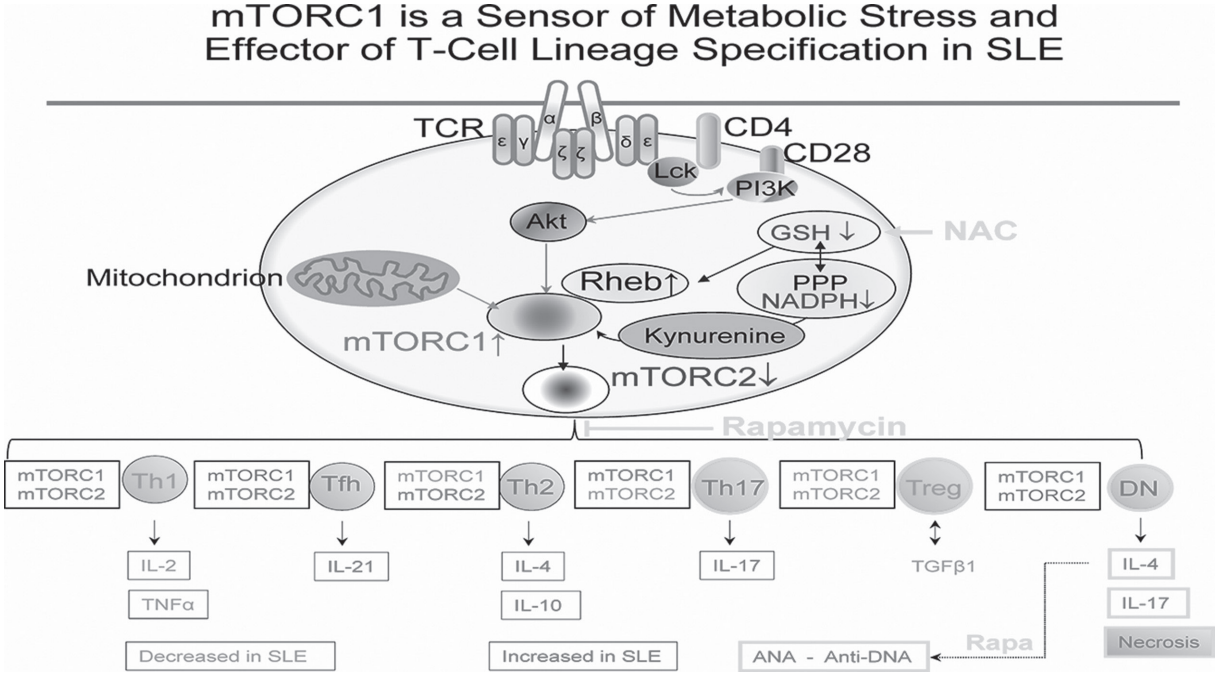

Abstract AI-29 Figure 1 mTORC1 is a Sensor of Metabolic Stress and Effector of T-Cell Lineage Specification in SLE. Metabolic stress is caused by imbalance between increased mitochondrial electron transport and diminished production of NADPH via the PPP. Impaired, NADPH-dependent metabolism of kynurenine activates mTORC1 which in turn leads to contraction of the TREGS and expands pro-inflammatory T-cell lineages such as TH1, TH17, TFH, and DNT cells. Rapamycin and NAC reverse T-cell skewing with clinical efficacy.

checkpoints in lupus pathogenesis. Blockade of mTORC1 has the premise of safe and effective treatment in SLE.

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Trial Registration Prospective Study of Rapamycin for the Treatment of SLE; ClinicalTrials.gov Identifier: NCT00779194. Treatment trial of SLE with N-acetylcysteine; ClinicalTrials.gov identifier: NCT00775476.

AI-30 GENDER DIFFERENCES IN PLASMA LEVELS OF ANA, ANTI-CD4, AND ANTI-DSDNA ANTIBODIES IN HEALTHY DONORS PRE AND POST FLU VACCINATION

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Background The ratio of females to males is 9:1 in for the prevalence of SLE in premenopausal women. Double strand anti-DNA (anti-dsDNA) autoantibodies are a diagnostic criteria for lupus and are believed to play a key role in SLE pathogenesis. In the current study, we investigated the presence and mechanisms of gender bias in autoantibody production in normal controls after influenza (flu) vaccination.

Materials and methods Plasma levels of anti-nuclear antibodies (ANA), anti-dsDNA autoantibodies, and anti-CD4 antibodies were assessed in a cohort of 5 healthy men and 11 healthy women. They were received flu vaccines during the 2012–2013 and 2013–2014 seasons. Blood draws were taken at 0, 7, and 14 days after vaccination. Vaccine responses were defined by neutralisation activities in plasma. Flu-specific antibody avidity was tested by ELISA. The levels of autoantibodies were analysed in plasma by ELISA

Results Women had higher levels of all 3 IgG autoantibodies compared to men at D0, but not flu-specific neutralising activities nor higher flu-specific antibody avidities. The median plasma levels of ANA antibodies (OD) at D0 were for men 0.2281 (IQR, 0.2058–0.2338), and for women 0.3697 (IQR, 0.2918–0.4261, p = 0.0005); the median plasma levels of anti-CD4 antibodies (OD) were 0.1678 (IQR, 0.1589–0.1932) and 0.2148 (IQR, 0.1986–0.2696p = 0.24); and the median plasma levels of anti-dsDNA antibody (IU/mL) were 122.3 (IQR, 91.86–175.8) and 197.3 (IQR, 131.2–389.8, p = 0.04), for men and women respectively. Influenza vaccination did not change the titer of autoantibodies at any time point. An autoantibody array also found significant differences in IgG autoantibodies at baseline between men and women. Anti-Ro, anti-Sm and anti-RNP antibodies increased at D14 post vaccination in women, but not men. The increases were not statistically significant.

Conclusions Women have increased levels of autoantibodies at baseline compared to men. Most autoantibody specificities are not impacted by vaccination, though some antibody specificities are increased in individual women post vaccination.

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